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REMARKS

Claims 13-23, 25, 27-31, 41, 42, 45 and 53-58 were pending in the above-identified application. By this Amendment, Applicants have amended claims 14, 15, 16, 20, 28, 29, 41 and 45, canceled claims 13, 17, 18, 19, 53, 54, 55, 56, 57 and 58 without disclaimer or prejudice to applicants' right to pursue these claims in the future, and added new claims 59-67. Accordingly, upon entry of this Amendment, claims 14-16, 20-23, 25, 27-31, 41, 42, 45 and 59-67 will be pending and under examination.

Support for new claim 59 may be found inter alia in the specification, as originally-filed, at page 58, line 33 through page 59, line 16; page 70, line 7 through page 78, line 10; page 82, line 29 through page 83, line 17; page 112, line 21 through page 114, line 8; page 167, line 31 through page 173, line 26; page 175, line 11 through page 177, line 5; and page 189, line 14 through page 193, line 11.

Support for new claim 60 may be found inter alia in the specification, as originally filed, at page 48, lines 15-21; and page 49, lines 2-8. Support for new claim 61 may be found inter alia in page 55, lines 14-35; and page 192, line 5 through 193, line 11. Support for new claim 62 may be found inter alia in the specification, as originally filed, at page 70, line 7 through page 74, line 5. Support for new claim 63 may be found inter alia in the specification, as originally filed, at page 74, line 7 through page 75, line 3. Support for new claim 64 may be found inter alia in the specification, as originally filed, at page 75, line 24 through page 76, line 29. Support for new claim 65 may be found inter alia in the specification,

as originally filed, at page 76, line 30 through page 78, line 10. Support for new claim 66 may be found inter alia in the specification, as originally filed, at page 82, line 29 through page 83, line 17. Support for new claim 67 may be found inter alia in the specification, as originally filed, at page 112, line 21 through page 114, line 8.

Applicants therefore maintain that new claims 59-67 raise no issue of new matter, are fully supported by the specification as originally-filed, and request entry of these claims.

Applicants note that the following objections and grounds for rejection have been indicated to have been withdrawn in the May 5, 2003 Final Office Action:

1. the objection to the claims as reciting an improper Markush group (par. 2);
2. the rejection under 35 U.S.C. § 112, first paragraph in paragraphs 5-8 of the last Office Action (par. 4);
3. the rejection under 35 U.S.C. § 112, second paragraph (par. 5);
4. the rejection under 35 U.S.C. § 102 in paragraphs 10-11 of the last Office Action (par. 6);
5. the rejection under 35 U.S.C. § 103 (par. 7); and
6. the obviousness type double patenting rejection in paragraphs 14-17 of the last Office Action (par. 8).

The following is a discussion of the new grounds of rejection set forth in the May 5, 2003 Final Office Action in paragraphs 9-13.

**35 U.S.C. 112, First Paragraph Rejections**

On pages 4-5 (par. 9-11), of the May 5, 2003 Office Action, the Examiner rejected claims 13 to 16, 20 to 23, 25, 27 to 31, 41, 42 and 45 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner alleged that the amendment to the definition of X where X is  $\text{NR}_3$  is not described in the specification for the genus.

The Examiner also rejected claims 13-17, 20-23, 25, 27-31, 41, 42, and 45 under 35 U.S.C. § 112, first paragraph, alleging that the definition of  $\text{R}_5$  where the aryl and heteroaryl of  $\text{R}_5$  can be substituted with the moieties  $\text{COR}_4$ ,  $\text{CO}_2\text{R}_4$ ,  $-\text{CON}(\text{R}_4)_2$ ,  $-\text{N}(\text{R}_4)_2$ ,  $-\text{OR}_4$ ,  $\text{SR}_4$ ,  $(\text{CH}_2)_6\text{OR}_4$ ,  $(\text{CH}_2)_6\text{SR}_4$ , which are not described in the specification for the genus. The Examiner required applicants to cancel the new matter in reply to this Office Action.

Further, the Examiner rejected claims 13-16, 20-23, 25, 27-31, 41, 42, and 45 under 35 U.S.C. § 112, first paragraph, as in the preceding paragraph.

In response, in an attempt to advance prosecution but without conceding the correctness of the Examiner's position, applicants have canceled claim 13 without disclaimer or prejudice, added new claim 59, and changed the dependency of certain claims from

claim 13 to claim 59. Claim 59 recites, "wherein X is S; O; or NR<sub>4</sub>."

Applicants maintain that new claim 59 is described in the specification as originally-filed, on page 58, line 33 through page 59, line 16; page 70, line 7 through page 78, line 10; page 82, line 29 through page 83, line 17; page 112, line 21 through page 114, line 8; page 167, line 31 through page 173, line 26; page 175, line 11 through page 177, line 5; and page 189, line 14 through page 193, line 11, and respectfully request that this ground of rejection be reconsidered and withdrawn.

In further response, applicants note that the definition of R<sub>5</sub> in claim 59 recites, wherein the aryl and heteroaryl of R<sub>5</sub> can be substituted with the following moieties: COR<sub>3</sub>; CO<sub>2</sub>R<sub>3</sub>; -CON(R<sub>3</sub>)<sub>2</sub>; CN; -NO<sub>2</sub>; N(R<sub>3</sub>)<sub>2</sub>; -OR<sub>3</sub>; -SR<sub>3</sub>; (CH<sub>2</sub>)<sub>o</sub>OR<sub>3</sub>; and (CH<sub>2</sub>)<sub>o</sub>SR<sub>3</sub>. Applicants maintain that new claim 59 is described in the specification, as originally-filed, on page 58, line 33 through page 59, line 16; page 70, line 7 through page 78, line 10; page 82, line 29 through page 83, line 17; page 112, line 21 through page 114, line 8; page 167, line 31 through page 173, line 26; page 175, line 11 through page 177, line 5; and page 189, line 14 through page 193, line 11, and respectfully request that this rejection be reconsidered and withdrawn.

### **35 U.S.C. 112, Second Paragraph**

On pages 5 to 10 (par. 12), of the May 5, 2003 Office Action, the Examiner rejected claims 13 to 15, 17, 18, 20 to 23, 25, 27 to 31, 41, 42, 45 and 53 to 58 under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to point out and distinctly claim the subject matter which applicant

regards as the invention.

In response, in an attempt to advance the prosecution but without conceding the correctness of the Examiner's position, applicants as noted above have canceled claims 13, 17, and 53-58 without disclaimer or prejudice, added new claim 59, and corrected claim dependencies from 13 to 59. Applicants further note that new claim 59 and other claims now pending do not recite "Z'" (see par. 12 (a)); do not recite "D" (see par. 12 (b)); do not recite "W" (see par. 12 (c)); and do not recite "R<sub>8</sub>" (see par. 12(d)). Applicants maintain that new claims 59 and claims dependent thereon are no longer subject to the grounds of rejection set forth in par. 12 (a)-(d) and request that these grounds of rejection be reconsidered and withdrawn.

In response to the rejection of claim 17 (par. 12 (e)), in an attempt to advance prosecution but without conceding the correctness of the Examiner's position, applicants have canceled claim 17 without disclaimer or prejudice and added new claim 60. In new claim 60, the nitrogen-containing hetero ring may be substituted as shown by R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub>, not R<sub>5</sub>, R<sub>6</sub> and R<sub>4</sub>. Applicants maintain that new claim 60 overcomes the ground of rejection and respectfully request that this ground of rejection be reconsidered and withdrawn.

In response to the rejection of claim 18 (par. 12(f)-(h)), in an attempt to advance prosecution but without conceding the correctness of the Examiner's position, applicants have canceled claim 18 without disclaimer or prejudice and added new independent claim 61.

Applicants maintain that new claim 61 overcomes the grounds of

rejection set forth in par. 12(f)-(h) and respectfully request that these grounds of rejections be reconsidered and withdrawn.

In response to the rejection of claim 53 (par. 12 (i)-(j))), in an attempt to advance prosecution but without conceding the correctness of the Examiner's position, applicants have canceled claim 53 without disclaimer or prejudice and added new independent claim 62. Applicants maintain that new claim 62 overcomes the grounds of rejection in paragraphs 12(i)-(j) and request the these grounds of rejection be reconsidered and withdrawn.

In response to the Examiner's rejection of claim 54 (par. 12(k)-(l)), in an attempt to advance prosecution but without conceding the correctness of the Examiner's position, applicants have canceled claim 54 without disclaimer or prejudice and added new independent claim 63. Applicants maintain that new claim 63 overcomes the grounds of rejection in paragraphs 12(k)-(l) and request that these grounds of rejection be reconsidered and withdrawn.

In response to the rejection of claim 51 (par. 12(m)-(o)), in an attempt to advance prosecution but without conceding the correctness of the Examiner's position, Applicants have canceled claim 55 without disclaimer or prejudice and added new independent claim 64. Applicants maintain that new claim 64 overcomes these grounds of rejection in paragraphs 12(m)-(o) and request that these rejections be reconsidered and withdrawn.

In response to the rejection of claim 56 (par. 12(p)-(r)), in an attempt to advance the prosecution but without conceding the correctness of the Examiner's position, applicants have canceled

claim 56 without disclaimer or prejudice and added new independent claim 65. Applicants maintain that new claim 65 overcomes the grounds of rejection in paragraphs 12(p)-(r) and request that these grounds of rejection be reconsidered and withdrawn.

In response to the rejection of claim 57 (par. 12(s)-(u)), in an attempt to advance prosecution but without conceding the correctness of the Examiner's position, applicants have canceled claim 57 without disclaimer or prejudice and added new independent claim 66. Applicants maintain that new claim 66 overcomes the grounds for rejection in paragraphs 12(s)-(u) and request that these grounds be reconsidered and withdrawn.

In response to the rejection of claim 58 (par. 12(v)-(x)), in an attempt to advance prosecution but without conceding the correctness of the Examiner's position, applicants have canceled claim 58 and added new independent claim 67. Applicants maintain that new claim 67 overcomes the grounds of rejection in paragraphs 12(v)-(x) and request that these grounds be reconsidered and withdrawn.

#### **Provisional Obviousness-Type Doubling Patenting Rejection**

On page 11 of the May 5, 2003 Office Action, the Examiner provisionally rejected claims 13 to 18, 20 to 23, 25, 27 to 31, 41, 42, 45 and 53 to 58 under the judicially created doctrine of obviousness-type double patenting as unpatentable over the claims of copending Application U.S. Serial No. 09/730,458. The Examiner stated that a terminal disclaimer could be used to "overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting



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application or patent is shown to be commonly owned with this application."

In response, applicants respectfully point out that where a "'provisional' double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that ground of rejection and permit the application to issue as a patent, thereby converting the 'provisional' double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent." See Manual of Patent Examining Procedure § 822.01, under the heading "Only Provisional Double Patenting Rejection Remaining In One Application." Applicants further point out that copending Application U.S. Serial No. 09/730,458 is not currently in condition for allowance. Therefore, applicants respectfully request that the Examiner reconsider and withdraw this provisional ground of rejection and permit this application to issue.

#### Supplemental Information Disclosure Statement

In paragraph 3 on page 2 of the May 5, 2003 Final Office Action, the Examiner reminded applicants that the information disclosure statement filed May 15, 2001 purportedly fails to comply with 37 C.F.R. §1.98(a)(2), and requested that copies of the listed references be submitted so that the list could be initialed and the record be completed.

In response applicants would like to direct the Examiner's attention to the following references which are listed on the attached Form PTO-1449 (**Exhibit A**) and are also listed below.

Copies of the references listed below are attached hereto as **Exhibits 1-12**. These references were previously submitted to, or cited by the Office in Application U.S. Serial No. 08/858,017, now U.S. Patent No. 6,245,773 B1, issued June 12, 2001, from which the subject application claims benefit under 35 U.S.C. § 120. These references were listed in May 15, 2001 information disclosure statement, submitted in connection with the subject application, but were not initialed by the Examiner.

1. Brown, et al., "Inhibitors of *Bacillus subtilis* DNA Polymerase III. 6-(Arylalkylamino) uracils and 6-Anilinouracils," *Journal of Medicinal Chemistry* (1977) 20(9): 1186-1189 (**Exhibit 1**);
2. Cho, H. et al., "Dihydropyrimidines: Novel Calcium Antagonists with Potent and Long-Lasting Vasodilative and Antihypertensive Activity," *Journal of Medicinal Chemistry* (1989) 32: 2399-2406 (**Exhibit 2**);
3. D'Eletto, R.D. and Javitt, N.B., "Effect of Doxazosin on Cholesterol Synthesis In Cell Culture," *Journal of Cardiovascular Pharmacology* (1989) 13, Supp. 2, S1-S4 (**Exhibit 3**);
4. Forray et al., "The  $\alpha_1$ -Adrenergic Receptor That Mediates Smooth Muscle Contraction in Human Prostate Has the Pharmacological Properties of the Clone Human  $\alpha_{1c}$  Subtype," *Molecular Pharmacology* (1994) 45: 703-708 (**Exhibit 4**);

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5. Khanina, E.L. et al., Alkylation of derivatives of 2-oxo-4-phenyl-6-methyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid. Chemical Abstracts 89: 43319 (1978) (Exhibit 5);
6. Mamaev, V.P. and Dubovenko, Z.D., Pyrimidines. XXI. 5-Substituted 2-hydroxy-4,6-diphenylpyrimidines. Chemical Abstracts 73: 77187 (1970) (Exhibit 6);
7. McGrath, J.C. et al., "Alpha\_Adrenoceptors: A Critical Review," Medicinal Research Reviews (1989) 9, No. 4, 401-533 (Exhibit 7);
8. Rovnyak, G.C. et al., "Dihydropyrimidine Calcium ChannelBlockers. 4. Basic 3-Substituted-4-aryl-1,4-dihydropyrimidine-5-carboxylic Acid Esters," Journal of Medicinal Chemistry (1992) 35(17): 3254-3263 (Exhibit 8);
9. Spiers, J.P. et al., "UK-52,046 (A Novel 1-Adrenoceptor Antagonist) and the Role of -Adrenoceptor Stimulation and Blockade on Atrioventricular Conduction, : Journal of Cardiovascular Pharmacology (1990) 16(5): 824-830 (Exhibit 9);
10. Triggle, D.J., "Dihydropyrimidine Calcium Channel Blockers. 2.3-Substituted-4-aryl-1,4-dihydro-6-methyl-5-pyrimidinecarboxylic Acid Esters as Potent Mimics of Dihydropyridines," Chemtracts- Organic Chemistry (Jan./Feb. 1991) 68-72 (Exhibit 10);

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11. Wetzel, J.M., et al., "Discovery of 1a-Adrenergic Receptor Antagonists Based on the L-Type Ca<sup>2+</sup> Channel Antagonist Niguldipine" Journal of Medicinal Chemistry(1995) 38(10): 1579-1581 (**Exhibit 11**); and
12. Zhan, G.L. et al., "Bunazosin Reduces Intraocular Pressure By Increasing Uveoscleral Outflow In Rabbits," Investigative Ophthalmology and Visual Science (1993) 34(4): Abst. No. 1133-49, p. 928 (**Exhibit 12**).

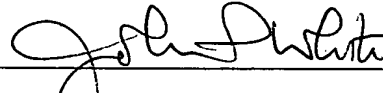
In summary, in light of the remarks made hereinabove, applicants respectfully request that the Examiner withdraw the various grounds of rejection set forth in the May 5, 2003 Office Action. If a telephone interview would be of assistance in advancing prosecution of the above-identified application, Applicants' undersigned attorney invites the Examiner to telephone him at the number provided.

If a telephone conversation would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

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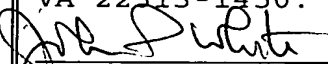
No fee, other than the enclosed fee of \$265.00 (\$55.00 for a one-month extension of time and \$210.00 for 5 additional independent claims), is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450.



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8/28/03  
Date